

IN THE CLAIMS

1. (CURRENTLY AMENDED) A bioreactor for producing functional cartilaginous tissue from a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate, comprising:

(a) a growth chamber; and

(b) means for applying hydrostatic fluid pressure and/or strain-controlled deformational loading via loading platens to the cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate,

wherein hydrostatic fluid pressure and/or strain-controlled deformational loading are controlled according to a loading regime optimized for cartilaginous tissue growth.

2. (ORIGINAL) The bioreactor of Claim 1, wherein the scaffold is bioresorable.

3. (ORIGINAL) The bioreactor of Claim 1, wherein the scaffold is biocompatible.

4. (ORIGINAL) The bioreactor of Claim 1, wherein the scaffold is biodegradable.

5. (ORIGINAL) The bioreactor of Claim 1, wherein the scaffold is non-bioresorable.

6. (CURRENTLY AMENDED) The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical hydrostatic fluid ~~pressurization~~ pressure.

7. (CURRENTLY AMENDED) The bioreactor of Claim 1 or 6, wherein the hydrostatic fluid ~~pressurization~~ is pressurized at from about 0 to about 18 MPa.

8. (CURRENTLY AMENDED) The bioreactor of Claim 7, wherein the hydrostatic fluid pressurization is pressurized at from about 0 to about 6 MPa.
9. (ORIGINAL) The bioreactor of Claim 6, wherein the cyclical frequency is from about 0 to about 5 Hz.
10. (ORIGINAL) The bioreactor of Claim 9, wherein the cyclical frequency is from about 0.1 to about 2 Hz.
11. (CURRENTLY AMENDED) The bioreactor of Claim 1, wherein the fluid pressurization pressure is applied for from about 0.5 to about 18 hours per day.
12. (CURRENTLY AMENDED) The bioreactor of Claim 11, wherein the fluid pressurization pressure is applied for from about 2 to about 6 hours per day.
13. (CURRENTLY AMENDED) The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical strain-controlled deformational loading.
14. (CURRENTLY AMENDED) The bioreactor of Claim 13, wherein the strain controlled deformational loading is from about 0 to about 50% strain, based upon the thickness of the cell-seeded scaffold.
15. (CURRENTLY AMENDED) The bioreactor of Claim 14, wherein the strain controlled deformational loading is from about 0 to about 20% strain.
16. (CURRENTLY AMENDED) The bioreactor of Claim 13, wherein the cyclical frequency of strain-controlled deformational loading is from about 0 to about 5 Hz.
17. (ORIGINAL) The bioreactor of Claim 16, wherein the cyclical frequency is from about 0.1 to about 2 Hz.

18. (CURRENTLY AMENDED) The bioreactor of Claim 13, wherein the strain-controlled deformational loading is from about 0.5 to about 18 hours per day.
19. (CURRENTLY AMENDED) The bioreactor of Claim 18, wherein the strain-controlled deformational loading is from about 2 to about 6 hours per day.
20. (CURRENTLY AMENDED) The bioreactor of Claim 1, wherein means (b) applies intermittent cyclical hydrostatic fluid ~~pressurization~~ pressure and intermittent strain controlled cyclical deformational loading.
21. (CURRENTLY AMENDED) The bioreactor of Claim 20, wherein the amplitude of the cyclical hydrostatic fluid pressure and the amplitude of the strain-controlled deformational loading are modified over time as matrix elaboration proceeds.
22. (ORIGINAL) The bioreactor of Claim 1, wherein the resulting tissue comprises hyaline cartilage.
23. (CURRENTLY AMENDED) The bioreactor of Claim 1, wherein the resulting tissue comprises hyaline cartilage and a an osteoconductive and/or osteoinductive substrate.
24. (ORIGINAL) The bioreactor of Claim 1, wherein the resulting tissue comprises elastic cartilage.
25. (ORIGINAL) The bioreactor of Claim 1, wherein the resulting tissue comprises fibrocartilage.
26. (ORIGINAL) The bioreactor of Claim 1, which comprises means for producing tissue in desired shapes.
27. (ORIGINAL) The bioreactor of Claim 26, wherein the shaped tissue conforms to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

28. (ORIGINAL) The bioreactor of Claim 1, wherein the loading platens which produce deformational loading conform to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

29. (CURRENTLY AMENDED) A method for producing functional cartilaginous tissue from a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate, said method comprising the steps of:

(a) inoculating chondrocytes or chondroprogenitors into a scaffold or a scaffold integrated with an osteoconductive and/or osteoinductive substrate;

(b) placing cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate into a bioreactor;

(c) filling said bioreactor with liquid growth medium;

(d) applying hydrostatic fluid pressurization and/or strain-controlled deformational loading to the cell-seeded scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate via a loading platens according to a loading regime optimized for cartilaginous tissue growth; and

(e) culturing said stressed cell-seed scaffold or cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate from step (d) for a time sufficient to produce functional cartilaginous tissue.

30. (ORIGINAL) The method of Claim 29, wherein the bioreactor is the bioreactor of Claim 1.

31. (ORIGINAL) The method of Claim 29, wherein the scaffold is biocompatible.

32. (ORIGINAL) The method of Claim 29, wherein the scaffold is biodegradable.

33. (ORIGINAL) The method of Claim 29, wherein the scaffold is non-biodegradable.

34. (ORIGINAL) The method of Claim 29, wherein the scaffold is bioresorbable.

35. (ORIGINAL) The method of Claim 29, wherein said stressed cells:  
(a) display enhanced maintenance of a chondrocyte phenotype; and  
(b) produce a functional cartilaginous matrix.

36. (ORIGINAL) The method of Claim 29, wherein hydrostatic pressurization is applied by means comprising a reservoir, a pump, and tubing interconnecting said growth chamber, said reservoir, and said pump, so as to allow pressurization of liquid growth medium from said reservoir, in response to force applied by said pump.

37. (ORIGINAL) The method of Claim 36, wherein said pump comprises a piston and chamber.

38. (ORIGINAL) The method of Claim 29, wherein in step (d) intermittent cyclical hydrostatic fluid pressurization is applied.

39. (CURRENTLY AMENDED) The method of Claim 38, wherein the hydrostatic fluid pressurization pressurized at is from about 0 to about 18 MPa.

40. (CURRENTLY AMENDED) The method of Claim 39, wherein the hydrostatic fluid pressurization pressurized at is from about 0 to about 6 MPa.

41. (ORIGINAL) The method of Claim 38, wherein the cyclical frequency is from about 0 to about 5 Hz.

42. (ORIGINAL) The method of Claim 41, wherein the cyclical frequency is from about 0.1 to about 2 Hz.

43. (ORIGINAL) The method of Claim 29, wherein the fluid pressurization is applied for from about 0.5 to about 18 hours per day.

44. (ORIGINAL) The method of Claim 43, wherein the fluid pressurization is applied for from about 2 to about 6 hours per day.

45. (CURRENTLY AMENDED) The method of Claim 29, wherein in step (d) intermittent cyclical strain-controlled deformational loading is applied.

46. (CURRENTLY AMENDED) The method of Claim 45, wherein the strain-controlled deformational loading is from about 0 to about 50% strain, based upon the thickness of the cell-seeded scaffold.

47. (CURRENTLY AMENDED) The method of Claim 46, wherein the deformational loading is from about 0 to about 20% strain.

48. (CURRENTLY AMENDED) The method of Claim 45, wherein the cyclical frequency of strain-controlled deformation loading is from about 0 to about 5 Hz.

49. (ORIGINAL) The method of Claim 48, wherein the cyclical frequency is from about 0.1 to about 2 hz.

50. (CURRENTLY AMENDED) The method of Claim 45, wherein the strain-controlled deformational loading is from about 0.5 to about 18 hours per day.

51. (CURRENTLY AMENDED) The method of Claim 50, wherein the strain-controlled deformational loading is from about 2 to about 6 hours per day.

52. (CURRENTLY AMENDED) The method of Claim 29, wherein in step (d) intermittent cyclical hydrostatic fluid ~~pressurization~~ pressure and intermittent cyclical strain-controlled deformational loading are applied.

53. (CURRENTLY AMENDED) The method of Claim 52, wherein the amplitude of the cyclical hydrostatic pressure and the amplitude of the deformational strain-controlled loading are modified over time as matrix elaboration proceeds.

54. (ORIGINAL) The method of Claim 29, wherein the resulting tissue comprises hyaline cartilage.

55. (ORIGINAL) The method of Claim 29, wherein the resulting tissue comprises hyaline cartilage and osteoinductive substrate.

56. (ORIGINAL) The method of Claim 29, wherein the resulting tissue comprises elastic cartilage.

57. (ORIGINAL) The method of Claim 29, wherein the resulting tissue comprises fibrocartilage.

58. (ORIGINAL) The method of Claim 29, wherein the bioreactor comprises means for producing tissue in desired shapes.

59. (ORIGINAL) The bioreactor of Claim 29, where the loading platens which produce deformational loading conform to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

60. (ORIGINAL) The method of Claim 59, wherein the shaped tissue conforms to a body part, a prosthesis, a cosmetic implant, or a defect to be filled.

61. (NEW) A bioreactor system for producing functional cartilaginous tissue, comprising:

(a) a cell-seeded scaffold or a cell-seeded scaffold integrated with an osteoconductive and/or osteoinductive substrate;

(b) a growth chamber; and

(c) means for applying hydrostatic fluid pressure and/or strain-controlled loading to a cell-seeded scaffold or a cell-seeded substance integrated with an osteoconductive and/or osteoinductive substance in the growth chamber via a loading platens,

wherein hydrostatic fluid pressure and/or strain-controlled deformational loading are controlled according to a loading regime optimized for cartilaginous tissue growth.